

Application No. 10/030,350  
Responsive to Restriction Requirement of September 16, 2003  
Amendment and Response filed March 16, 2004

**Listing of Claims.**

**Claims 1-20 (cancelled).**

**Claim 21 (previously cancelled).**

**Claim 22 (currently amended):** Process A method for the preparation of cells suitable for transplantation into a mammal, which cells are capable of forming amyloid deposits, said method process comprising contacting the cells *in vitro* with an inhibitor of amyloid deposit formation.

**Claim 23 (currently amended):** Process The method according to claim 22, wherein said inhibitor causes breakdown of amyloid deposits, the deposits having been formed by said cells prior to said contacting.

**Claim 24 (currently amended):** Process The method according to claim 22, in which the wherein said cells are cultured in the presence of the inhibitor.

**Claim 25 (previously cancelled).**

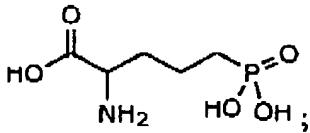
**Claim 26 (previously cancelled).**

**Claim 27 (currently amended):** Process The method according to claim 22, wherein the inhibitor is said inhibitor comprises a compound selected from the group consisting of

(i) 3-(3-hydroxy-1-propyl)amino-1-propansulfonic acid.

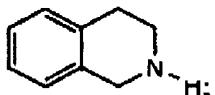
HOCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>SO<sub>3</sub>H;

(ii) DL-2-amino-5-phosphovaleric acid

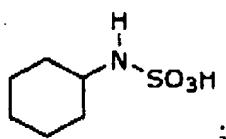


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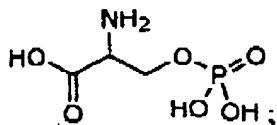
(iii) 1,2,3,4-tetrahydroisoquinoline



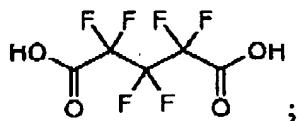
(iv) cyclohexylsulfamic acid



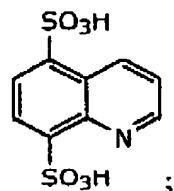
(v) O-phospho-L-serine



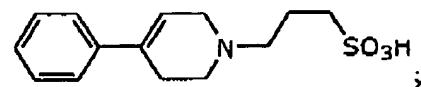
(vi) hexafluoroglutaric acid



(vii) 8-methoxyquinoline-5-sulfonic acid

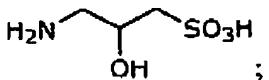


(viii) 4-phenyl-1-(3'-sulfopropyl)-1,2,3,6-tetrahydropyridine

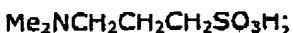


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(ix) 3-amino-2-hydroxy-1-propanesulfonic acid



(x) 3-dimethylamino-1-propanesulfonic acid



and pharmaceutically acceptable esters, acids, and salts or a salt thereof.

Claim 28 (previously cancelled).

Claim 29 (previously cancelled).

Claim 30 (previously cancelled).

Claim 31 (previously cancelled).

Claim 32 (currently amended): A culture medium or a culture medium pre-mix ~~which comprises an inhibitor or comprising a compound as defined in claim 27.~~

Claim 33 (original): A culture of cells in which the culture medium is as defined in claim 32.

Claim 34 (original): A culture according to claim 33 in which the cells are islet cells.

Claim 35 (currently amended): *Ex vivo* cells prepared by ~~a process the method~~ according to claim 22.

Claim 36 (currently amended): *Ex vivo* cells according to claim 35, wherein said cells are in a preparation ~~that comprises an inhibitor or comprising an inhibitor, wherein said inhibitor comprises a compound selected from the group consisting of~~

- (i) 3-(3-hydroxy-1-propyl)amino-1-propanesulfonic acid;
- (ii) DL-2-amino-5-phosphovaleric acid;
- (iii) 1,2,3,4-tetrahydroisoquinoline;
- (iv) cyclohexylsulfamic acid;
- (v) *O*-phospho-L-serine;

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(vi) hexafluoroglutaric acid;  
(vii) 8-methoxyquinoline-5-sulfonic acid;  
(viii) 4-phenyl-1-(3'-sulfopropyl)-1,2,3,6-tetrahydropyridine;  
(ix) 3-amino-2-hydroxy-1-propanesulfonic acid; ~~or~~  
(x) 3-dimethylamino-1-propanesulfonic acid;  
and pharmaceutically acceptable esters, acids, and salts ~~or~~ a salt thereof.

Claim 37 (previously cancelled). 

Claim 38 (previously cancelled). 

Claim 39 (previously cancelled). 

Claim 40 (previously cancelled). 

Claim 41 (previously amended): A pharmaceutical composition comprising a cell according to claim 35 and a pharmaceutically acceptable carrier or diluent.

Claim 42 (previously cancelled). 

Claim 43 (currently amended): A vessel for containing a culture of cells, ~~which wherein~~ ~~said~~ vessel is coated with ~~an inhibitor~~ or a compound as defined in claim 3 claim 22.

Claim 44 (previously amended): A kit for culturing cells comprising a culture medium or culture medium pre-mix as defined in claim 32.

Claim 45 (previously cancelled). 

Claim 46 (currently amended): Method A method of identifying an inhibitor that can be used to prepare cells for transplantation in a process ~~the method~~ according to claim 22, comprising contacting a candidate substance with a mammalian cell and determining whether the candidate substance inhibits the formation of fibrils or causes the breakdown of fibrils, ~~(i) the inhibition of formation of fibrils or (ii) the breakdown of fibrils,~~ ~~indication indicating~~ that the substance is an inhibitor that can be used in said process.

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**Claim 47 (previously amended): Method A method** of identifying an inhibitor that can be used to prepare cells for transplantation in a process ~~the method~~ according to claim 22, comprising contacting a candidate substance with a protein capable of forming fibrils, or with a fibril, and determining whether the substance inhibits the formation of the protein into a fibril, or whether the substance causes the breakdown of fibrils ~~the fibril~~, (i) ~~inhibition of fibril formation or, (ii) the breakdown of fibrils~~, indicating that the substance can be used in said process.

**Claim 48 (previously cancelled).**

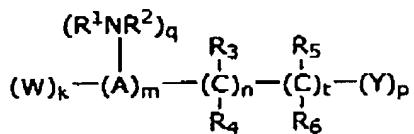
**Claim 49 (previously cancelled).**

**Claim 50 (previously cancelled).**

**Claim 51 (previously cancelled).**

**Claim 52 (previously cancelled).**

**Claim 53 (new):** The method according to claim 22, wherein said inhibitor comprises a compound according to the formula



wher cin

k, m, t, p and q are independently 0 or 1;

n is an integer from 0 to 3;

C is a carbon;

N is a nitrogen;

W is hydrogen or an anionic group at physiological pH;

Y is an anionic group at physiological pH;

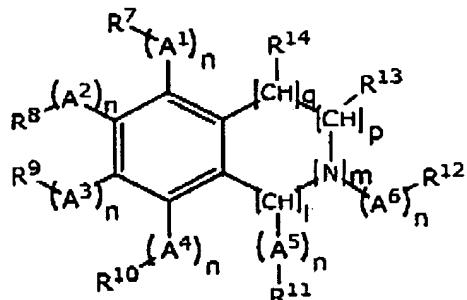
R<sup>1</sup> and R<sup>2</sup> are independently hydrogen, alkyl, an anionic group at physiological pH, or R<sup>1</sup> and R<sup>2</sup>, taken together with the nitrogen to which they are attached, may form an unsubstituted or substituted heterocycl having from 3 to 7 atoms in the heterocyclic ring;

R<sup>3</sup> hydrogen, halogen, thiol or hydroxyl;

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$R^4$ ,  $R^5$ , and  $R^6$  are independently hydrogen or halogen; and  
 $A$  is hydrogen or  $C_1$  to  $C_6$  alkyl;  
 and pharmaceutically acceptable esters, acids, and salts thereof.

**Claim 54 (new):** The method according to claim 22, wherein said inhibitor comprises a compound according to the formula



wherein

C is a carbon;

N is a nitrogen;

H is a hydrogen;

$A^1$ ,  $A^2$ ,  $A^3$ ,  $A^4$ ,  $A^5$  and  $A^6$  are independently alkyl, O, S, or -NH;

$m$  and  $n$  (for each individual A group) are independently 0 or 1;

$p$ ,  $q$  and  $l$  are independently 0, 1, or 2;

$R^2$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and each  $R^{14}$  are independently hydrogen, alkyl, alicyclyl, heterocycl or aryl, each  $R^{13}$  is independently hydrogen, alkyl, alicyclyl, heterocycl, aryl or an anionic group, and adjacent R groups may form an unsubstituted or substituted cyclic or heterocyclic ring;

and pharmaceutically acceptable esters, acids, and salts thereof.

**Claim 55 (new):** The method according to claim 22, wherein the cells are islet, liver, muscle, kidney, neuronal, or stem cells.

**Claim 56 (new):** The method according to claim 22, wherein the cells are human, primate, rodent, rabbit, ovine, porcine, feline, or canine cells.

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*CG*  

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**Claim 57 (new):** The method according to claim 22, wherein the amyloid deposits comprise islet amyloid polypeptide, A $\beta$  peptide, prion protein, immunoglobulin light chain, amyloid A protein, transthyretin, cystatin,  $\beta$ 2-microglobulin, apolipoprotein A-1, gelsolin, calcitonin, atrial natriuretic factor, lysozyme variants, insulin, or fibrinogen.

**Claim 58 (new):** The method according to claim 22, wherein the cells are islet cells and the deposits comprise islet amyloid polypeptide.

[“Remarks/Arguments” on following page.]